REMARKS

Claims 1, 2, 4, 9, 10, 12023, 38, 40, 42, 44 and 45 are currently under examination. The following addresses the substance of the Office Action.

Non-obviousness

The Examiner has rejected Claims 1, 2, 9, 10, 13, 13, 16, 17, 38, 40, and 42-45 under 35 USC §103(a) as being allegedly unpatentable over Anthony et al. (*J. Clin. Microbiol.* 2000 **38**:781-788) in view of Bamdad *et al.* (USP 6,541,617). More specifically, the Examiner alleges that it would have been obvious to one skilled in the art at the time the invention was made to modify the method of Anthony by using a spacer of at least 40 bases in length as taught by Bamdad *et al.*

> To establish a *prima facie* case of obviousness, the PTO must cite one or more references that provide some suggestion or motivation to modify the references to achieve the claimed invention, provide a reasonable expectation of success to achieve the claimed invention, and finally, the cited art must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Here, the cited art either taken alone or in combination, fails to provide any of the required factors.

The present invention is related to a method of using arrays comprising covalently bound capture nucleotide sequences wherein these sequences comprise a spacer and a sequence that specifically binds to the target; two categories of capture nucleotides sequences for group and sub-group detection and primer pairs capable of amplifying at least two of 4 homologous sequences. In Claim 1, these single-stranded capture nucleotides sequences are covalently bound to the solid support and include a spacer that places the specific sequence of the capture nucleotide sequence such that it is able to hybridize with the corresponding target nucleotide sequence at a certain distance from the solid support surface (at least 40 bases). The binding between the target nucleotide sequence and its corresponding capture nucleotide sequence forms a signal at the expected location (the location of the specific capture nucleotide sequence), the detection of said signal allowing a discrimination of a target sequence from other homologous sequences obtained from other organisms.

As discussed in the response to the previous Office Action, mailed March 18, 2005, in contrast to the presently claimed method in which the capture nucleotide sequences are covalently bound to an insoluble support by a spacer, Anthony et al. teaches the use of short

capture probes of 20-25 bases which do not include a spacer and are immobilized on nylon membranes. The binding of the capture probes on filter or membrane means that there is no control of which part of the sequence would be available for hybridization (Anthony et al. pg. 783, line 2: "The length of the UV exposure used to link the probe on the nylon was found to have a marked effect on the intensity of the resulting spots"). Therefore, because there is no single point attachment of capture probes on nylon membranes, the addition of a spacer to the capture probes is not compatible with the method of Anthony et al. In contrast to the method of Anthony, the utilization of spacers in the present method ensures that the portions of the capture nucleotide sequences which are complementary to the target sequences are available for hybridization. Therefore, Anthony in fact teaches away from the present invention.

Additionally, in the method of Anthony et al. one target sequence can cross-react with several capture probes (note that some of the filters depicted in Fig. 1 of the Anthony reference contain more than one position of hybridization). In such cases, it is the pattern of several positive spots which allows specific identification of the organism present. This means that the interpretation of the result is not straightforward. Contrary to method which utilize a pattern of spots (i.e. Anthony et al.), in the embodiment of Claim 45 a single "spot signal" directly allows the identification of a specific organism, therefore one capture nucleotide sequence is sufficient for the identification of one target nucleotide sequence thus permitting correlation between intensity of the spot signal and the amount of target nucleotide sequence present.

Furthermore, as is stated in the Declaration under 37 CFR 1.131, submitted herewith, the claimed invention was completed in a WTO country prior the date that appears on Anthony et al. publication. Therefore, Applicants assert that the cited reference is NOT PRIOR ART for the currently pending claims.

Bamdad *et al.* alone does not disclose all the limitations of the claimed invention.

Therefore, Claims 1, 2, 9, 10, 13, 13, 16, 17, 38, 40, and 42-45 are not obvious over the cited references and their rejection under 35 USC §103(a) should be withdrawn.

The Examiner has rejected Claim 15 under 35 USC §103(a) as being allegedly unpatentable over Anthony et al. (*J. Clin. Microbiol.* 2000 **38**:781-788) in view of Bamdad *et al.* (USP 6,541,617) as applied to Claims 1, 2, 9, 10, 13, 13, 16, 17, 38, 40, and 42-45 above, and further in view of Vannuffel et al. (WO 99/16780). More specifically, the Examiner alleges that

because Vannuffel et al. teaches the detection of the *FemA* gene of *Staphylococci* species, it would have been obvious to combine this teaching with the method of Anthony et al. as modified by using a spacer of at least 40 bases in length as taught by Bamdad *et al.*

Vannuffel's disclosure of the use of the *FemA* gene of *Staphylococci* species to detect bacteria present in a sample does not provide motivation to combine arrays comprising covalently bound probes of the lengths recited in the claims which comprise a spacer of at least 40 nucleotides in length, and primer pairs capable of amplifying at least two of 4 homologous sequences in methods for detecting specific nucleotide sequences having a homology level higher than 60% with sequences from other organisms. Furthermore, Vannuffel fails to cure the deficiencies of Anthony et al. (as not being prior art for the currently pending claims) combined with Bamdad *et al.* as discussed with regards to Claims 1, 2, 9, 10, 13, 13, 16, 17, 38, 40, and 42-45 above. Thus, Vannuffel *et al.* fails to correct the failure of Anthony *et al.* and Bamdad *et al.* to render the claimed invention obvious for the reasons addressed above. Therefore, dependent Claim 15 is also non-obvious.

The Examiner has rejected Claim 18 under 35 USC §103(a) as being allegedly unpatentable over Anthony et al. (*J. Clin. Microbiol.* 2000 **38**:781-788) in view of Bamdad *et al.* (*USP 6,541,617*) as applied to Claims 1, 2, 9, 10, 13, 13, 16, 17, 38, 40, and 42-45 above and further in view of Boon et al. (USP 6,488,932). More specifically, the Examiner alleges that because Boon et al. teach that it is advantageous to detect individual sequences that belong to MAGE family for the diagnosis of tumors, it would have been obvious to combine this teaching with the method of Anthony et al. as modified by using a spacer of at least 40 bases in length as taught by Bamdad *et al.*.

Boon's disclosure of the use of the MAGE family to diagnose tumors does not provide motivation to combine arrays comprising covalently bound probes of the lengths recited in the claims which comprise a spacer of at least 40 nucleotides in length, and primer pairs capable of amplifying at least two of 4 homologous sequences in methods for detecting specific nucleotide sequences having a homology level higher than 60% with sequences from other organisms. As discussed above, Anthony et al. is not prior art for currently pending claims and Bamdad *et al.* alone does not disclose all the limitations of the claimed invention. Boon *et al.* fails to correct

the failure of Anthony *et al.* and Bamdad *et al.* to render the claimed invention obvious for the reasons addressed above. Therefore, dependent Claim 18 is also non-obvious.

The Examiner has rejected Claims 20 and 22 under 35 USC §103(a) as being allegedly unpatentable over Anthony et al. (*J. Clin. Microbiol.* 2000 **38**:781-788) in view of Bamdad *et al.* (USP 6,541,617) as applied to Claims 1, 2, 9, 10, 13, 13, 16, 17, 38, 40, and 42-45 above and further in view of Klein et al. (USP 6,255,059). More specifically, the Examiner alleges that because Klein teaches that it is advantageous to detect sequences that belong to the dopamine of histamine receptors coupled to the G genes family to mediate transmembrane signaling by external stimuli, endocrine function, carbohydrate metabolism, etc., it would have been obvious to combine this teaching with the method of Anthony et al. as modified by using a spacer of at least 40 bases in length as taught by Bamdad *et al.*.

Klein's disclosure of the use of sequences that belong to the dopamine of histamine receptors coupled to the G genes family to mediate transmembrane signaling by external stimuli, endocrine function, carbohydrate metabolism, etc. does not provide motivation to combine arrays comprising covalently bound probes of the lengths recited in the claims which comprise a spacer of at least 40 nucleotides in length, and primer pairs capable of amplifying at least two of 4 homologous sequences in methods for detecting specific nucleotide sequences having a homology level higher than 60% with sequences from other organisms. As discussed above, Anthony et al. is not prior art for currently pending claims, while Bamdad *et al.* alone does not disclose all the limitations of the claimed invention. Klein *et al.* fails to correct the failure of Anthony *et al.* and Bamdad *et al.* to render the claimed invention obvious for the reasons addressed above. Therefore, dependent Claims 20 and 22 are also non-obvious.

The Examiner has rejected Claim 21 under 35 USC §103(a) as being allegedly unpatentable over Anthony et al. (*J. Clin. Microbiol.* 2000 **38**:781-788) in view of Bamdad *et al.* (USP 6,541,617) as applied to Claims 1, 2, 9, 10, 13, 13, 16, 17, 38, 40, and 42-45 above and further in view of Murphy et al. (WO 94/05695). More specifically, the Examiner alleges that because Murphy teaches that it is advantageous to detect sequences that belong to the choline receptors coupled to the G genes family for use in diagnosis of neurological, viral or endocrine pathologies, it would have been obvious to combine this teaching with the method of Anthony et al. as modified by using a spacer of at least 40 bases in length as taught by Bamdad *et al.*.

Murphy's disclosure of the use of sequences that belong to the choline receptors coupled to the G genes family for use in diagnosis of neurological, viral or endocrine pathologies does not provide motivation to combine arrays comprising covalently bound probes of the lengths recited in the claims which comprise a spacer of at least 40 nucleotides in length, and primer pairs capable of amplifying at least two of 4 homologous sequences in methods for detecting specific nucleotide sequences having a homology level higher than 60% with sequences from other organisms. As discussed above, Anthony et al. is not prior art for currently pending claims, while Bamdad *et al.* alone does not disclose all the limitations of the claimed invention. Murphy *et al.* fails to correct the failure of Anthony *et al.* and Bamdad *et al.* to render the claimed invention obvious for the reasons addressed above. Therefore, dependent Claim 21 is also non-obvious.

The Examiner has rejected Claim 23 under 35 USC §103(a) as being allegedly unpatentable over Anthony et al. (*J. Clin. Microbiol.* 2000 **38**:781-788) in view of Bamdad *et al.* (USP 6.541,617) as applied to Claims 1, 2, 9, 10, 13, 13, 16, 17, 38, 40, and 42-45 above and further in view of Waxman et al. (USP 6,207,648). More specifically, the Examiner alleges that because Waxman teaches that it is advantageous to detect sequences that belong to the cytochrome P450 isoforms family for use in treatment of cancer, it would have been obvious to combine this teaching with the method of Anthony et al. as modified by using a spacer of at least 40 bases in length as taught by Bamdad *et al.*.

Waxman's disclosure of the use of sequences that belong to the cytochrome P450 isoforms family for use in treatment of cancer does not provide motivation to combine arrays comprising covalently bound probes of the lengths recited in the claims which comprise a spacer of at least 40 nucleotides in length, and primer pairs capable of amplifying at least two of 4 homologous sequences in methods for detecting specific nucleotide sequences having a homology level higher than 60% with sequences from other organisms. As discussed above, Anthony et al. is not prior art for the currently pending claims, while Bamdad *et al.* alone does not disclose all the limitations of the claimed invention. Waxman *et al.* fails to correct the failure of Anthony *et al.* and Bamdad *et al.* to render the claimed invention obvious for the reasons addressed above. Therefore, dependent Claim 23 is also non-obvious.

CONCLUSION

In view of the foregoing, Applicants respectfully submit the present application is fully in condition for allowance. If any issues remain that may be addressed by a phone conversation, the Examiner is invited to contact the undersigned at the phone number listed below.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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